UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/232,880	01/15/1999	JIANGCHUN XU	210121.428C6	8285

500 7590 09/27/2002

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	21

DATE MAILED: 09/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/232,880	Applicant(s) XU ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,11-25,27-30 and 34-37* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 13-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on April 2, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/232,880 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 1-6, 8, 9, 11-25, 27-30 and 34-37 are pending.

Claims 1-6 and 13-25, drawn to non-elected inventions are withdrawn from examination.

Claims 26, 31-33, 38 and 39 have been canceled.

Claims 27-30 and 34-37 have been amended.

Claims 8, 9, 11, 12, 27-30 and 34-37 are examined on the merits.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

3. The rejection of claims 8, 9, 11, 12, 27-30 and 34-37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

4. The rejection of claims 8, 9, 11, 12, 27, 28-30 and 34-37 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn. Claims 26, 31-33, 38 and 39 have been cancelled.

Claim Rejections - 35 USC § 102

5. The rejection of claims 8, 9, 11 and 12 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,786,148 (filed November 5, 1996) is withdrawn in view of the cancellation of claims 26, 32, 33 and 39.

Claim Rejections - 35 USC § 103

6. The rejection of claims 8, 9, 11 and 12 under 35 U.S.C. 103(a) as being unpatentable over WO 98/45420 (October 15, 1998) is withdrawn in view of the cancellation of claims 31 and 38.

Grounds of Rejection

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 8, 9, 11, 12, 27-30 and 34-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well established utility.

Claims 8, 9, 11, 12, 27-30 and 34-37 are broadly drawn to methods of determining the presence or absence of prostate cancer comprising contacting a

biological sample obtained from a patient with an oligonucleotide that hybridizes to any one of SEQ ID NO: 67, 107, 308 or 311. These diagnostic methods include for example hybridization techniques, polymerase chain reaction, as well as reverse transcription polymerase chain reaction. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to prostate cancer, see page 38, lines 6-16. Applicants have disclosed in the specification that SEQ ID NO: 107 also identified as F1-12 and P504S is over-expressed in 60% of prostate tumors, however detectable in normal kidney and not detectable in other tissues tested, see page 48, lines 10-12. The specification also states that the said sequence was highly expressed in 2 prostate tumors tested; but undetectable in other tested tissues, see page 48, lines 25 and 26. This is contradictory to information presented in lines 10-12 of the same page. On page 51, lines 18-20 of the specification it is disclosed that "P80 [mRNA also regarded as SEQ ID NO: 6] was found to be over-expressed in prostate (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor." Both cDNAs, SEQ ID NO: 308 (P712P) and SEQ ID NO: 311 (novel 27) "...showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues." , see page 53, lines 9-11. "Clones...P712P.. showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.", see page 53, lines 11-16. These results do not support Applicants' asserted use of the claimed methods

for detection of any prostate disorders, particularly prostate cancer. There is no disclosure or working examples that demonstrate the specifically asserted utility and evidences a substantial utility was well established at the time of filing. Applicants have provided information that simply supports the fact that SEQ ID NO: 67, 107, 308 and 311 is detectable in many tissue and possibly exclusively in prostate. There is no information supporting the use of the listed sequences as a specific tumor marker to be implemented in the broadly claimed methods. The specification does not exemplify the use of any of the said sequences in differential expression in normal prostate tissue versus high risk (potentially diseased) prostate tissue/ prostate cancer tissue or their reliability as biomarkers, which may signal a stage of carcinogenesis. Based on the analysis set forth above the specification does not exemplify sufficient findings that constitute a specific, substantial or credible utility.

Claims 8, 9, 11, 12, 27-30 and 34-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 8, 9, 11, 12, 27-30 and 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 8, 9, 11, 12, 27-30 and 34-37 are broadly drawn to methods of determining the presence or absence of prostate cancer comprising contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to any one of SEQ ID NO: 67, 107, 308 or 311. These diagnostic methods include for example hybridization techniques, polymerase chain reaction, as well as reverse transcription polymerase chain reaction. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to prostate cancer. These diagnostic methods include for example hybridization techniques, polymerase chain reaction, as well as reverse transcription polymerase chain reaction.

Applicants have designated the target sequences as SEQ ID NO: 67 (P80), SEQ ID NO: 107 (F1-12 or P504S), SEQ ID NO: 308 (P712P) and SEQ ID NO: 311 (novel 27). The specification asserts that the said target sequences were found in various tissues, especially prostate tissues. However, the obtained results set forth in the specification on page 48, lines 10-12, 25 and 26; page 51, lines 18-20; page 53, lines 9-16 are not indicative of prostate cancer, but possibly tissue typing. Even if tissue typing was considered to be a valid utility the specification is not enabled. The specification does not enable one of ordinary skill in the art to definitively assess the incidence of any

type of cancer, particularly prostate cancer in a test sample. And while the evidence presented in the specification does point to the high occurrence of the listed sequences in prostate tissues, this is not sufficient in implementing the said sequences in a molecular based diagnostic method for prostate cancer with the said sequences. Furthermore, Applicants have not provided any disclosure enabling the use of oligonucleotides that hybridize to small sections of SEQ ID NO: 67, 107, 308 and 311. There is no disclosure designating what fragments of the sequences bound by oligonucleotides in the method that could be regarded as enabling one of ordinary skill in the art to use the said sequences in any diagnostic method. The experimental design presented in the specification lacks information regarding the applicability of SEQ ID NO: 67, 107, 308 and 311 and bound sections of the sequences in diagnostic methods relative to prostate cancer. Given the differing hybridization patterns listed in the 101 rejection, paragraph number 7 it is not reasonable to conclude that each of the sequences and their sequences bound by oligonucleotides would be effective in yielding a discriminate diagnosis between distinct disorders.

Applicants have not set forth any supporting evidence that suggests that any of the sequences (SEQ ID NO: 67, 107, 308 and 311) are unique tumor or molecular markers for prostate cancer. Similarly, the test samples to be used in the methods do not encompass sources from prostate tissue itself. In addition, the molecular-based techniques presented in the specification do not take into account the possibility that results from such diagnostic tests can be obscured by the presence of excess normal DNA. Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S110, 1999) reports on diagnostic methods in the realm of pancreatic tissue, however this review article is relevant to Applicants' claimed invention. It is art known that molecular–based assays are valid tools used in predicting and detecting diseases, however as assessed in the Tascilar review "...these tests should be interpreted with caution...". and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Furthermore, Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as

markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder is highly speculative and unpredictable.

Based on the analysis and the teachings presented above it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

11. Claims 8, 9, 11, 12, 27-30 and 34-37 are free of the art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
September 26, 2002